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     (FILE 'HOME' ENTERED AT 11:14:35 ON 01 OCT 2008)

     FILE 'REGISTRY' ENTERED AT 11:16:55 ON 01 OCT 2008
L1             1 S QUETIAPINE/CN
L2          2017 S 3068.74.6/RID
L3       1191226 S 46.383.1/RID
L4           518 S L2 AND L3
L5           321 S NRS=2 AND L4
L6          1540 S  C19 H21 N3 O S/MF
L7             5 S L5 AND L6
L8         16934 S 1-PIPERAZINEETHANOL
L9             1 S L7 AND L8

     FILE 'CAPLUS' ENTERED AT 11:21:05 ON 01 OCT 2008
L10            9 S L9
L11         1131 S L1
L12            7 S L10 AND L11
L13            9 S L12 OR L10

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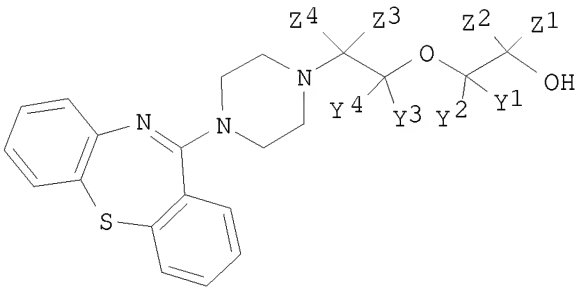
L13 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:674294 CAPLUS
DOCUMENT NUMBER: 149:32336
TITLE: Preparation of dibenzothiazepine derivatives as antagonists of multiple neurotransmitter receptors
INVENTOR(S): Tung, Roger; Harbeson, Scott
PATENT ASSIGNEE(S): Concert Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 35pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008066620	A2	20080605	WO 2007-US22338	20071019

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2006-853209P P 20061020
OTHER SOURCE(S): MARPAT 149:32336
GI



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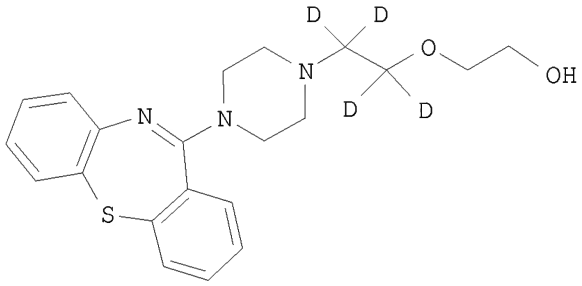


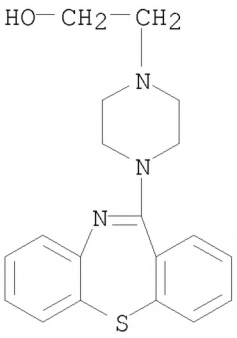
II

AB This title compds. with general formula I [wherein Z1-Z4 = independently hydrogen or deuterium; Y1-Y4 = independently hydrogen, deuterium, or fluorine; and at least one of Z1-Z4 is deuterium] or pharmaceutically acceptable acid addition salts, solvates, hydrates, or polymorphs thereof were prepared as antagonists of multiple neurotransmitter receptors in brain, for the treatment of diseases and conditions beneficially from the inhibition of serotonergic 5HT1A and 5HT2 receptors, dopaminergic D1 and D2 receptors, histaminergic H1 receptors, or adrenergic α1 and α2 receptors. For example, compound II was prepared in a multi-step synthesis. I can be used for the treatment of a patient suffering from or susceptible to a disease of condition selected from schizophrenia, schizo-affective disorders, mania (manic disorder), bipolar I disorder, bipolar II disorder, depression associated with bipolar disorders, etc.

IT 329216-67-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dibenzothiazepine derivs. as antagonists of multiple neurotransmitter receptors)

RN 329216-67-3 CAPLUS

CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)


HO
CH2
CH2
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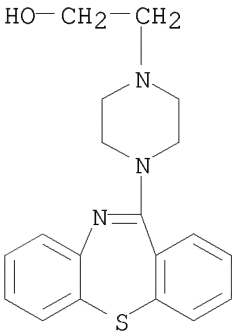
L13 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:79719 CAPLUS
DOCUMENT NUMBER: 148:363066
TITLE: Identification, isolation, synthesis and characterization of impurities of quetiapine fumarate
AUTHOR(S): Bharathi, Ch.; Prabahar, K. J.; Prasad, Ch. S.; Srinivasa Rao, M.; Trinadhachary, G. N.; Handa, V. K.; Dandala, Ramesh; Naidu, A.
CORPORATE SOURCE: Research Centre, Aurobindo Pharma Ltd., Hyderabad, 500072, India
SOURCE: Pharmazie (2008), 63(1), 14-19
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB In the process for the preparation of quetiapine fumarate (1), six unknown impurities (I-VI) and one known impurity (intermediate) were identified ranging from 0.05-0.15% by reverse-phase HPLC. These impurities were isolated from crude samples using reverse-phase preparative HPLC and characterized based on the spectral data. The known impurity was an intermediate, 11-piperazinyldibenzo[b,f][1,4]thiazepine(piperazinylthiazepine). The structures were established unambiguously by independent synthesis and coinjection in HPLC to confirm the retention times. To the best of authors' knowledge, these impurities have not been reported before. Structural elucidation of all impurities by spectral data (1H NMR, 13C NMR, MS and IR), synthesis and formation of these impurities are discussed in detail.

IT 329216-67-3P
RL: OCU (Occurrence, unclassified); SPN (Synthetic preparation); OCCU (Occurrence); PREP (Preparation)
(identification, isolation, synthesis and characterization of impurities of quetiapine fumarate)

RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:249111 CAPLUS
DOCUMENT NUMBER: 147:541911
TITLE: Process for the preparation of quetiapine, a dopamine antagonist
INVENTOR(S): Deshpande, Pandurang Balwant
PATENT ASSIGNEE(S): Orichid Chemicals & Pharmaceuticals Ltd., India
SOURCE: Indian Pat. Appl., 26pp.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2003CH00804	A	20051118	IN 2003-CH804	20031006
PRIORITY APPLN. INFO.:			IN 2003-CH804	20031006

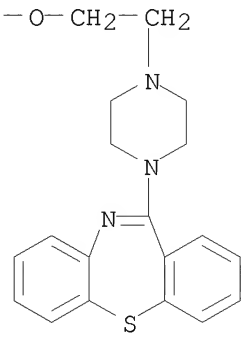
OTHER SOURCE(S): CASREACT 147:541911
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

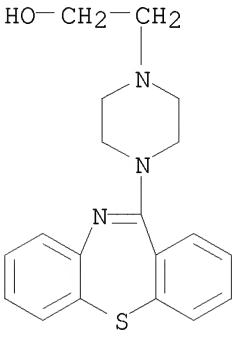
AB The present invention relates to a process for the preparation of biol. active thiazepine derivative I [R1 = (CH2)2O(CH2)2OH, (CH2)2OH, (CH2)2Cl]. The present invention more particularly relates to an improved process for the preparation of quetiapine [I; R1 = (CH2)2O(CH2)2OH], a dopamine antagonist. Thus, reaction of 2-fluoronitrobenzene with thiosalicylic acid followed by converting the resulting 2-(2-nitrophenylthio)benzoic acid into acid chloride, reacting the acid chloride with 1-[2-(2-hydroxyethoxy)ethyl]piperazine, reduction of II, and cyclization of III afforded quetiapine [I; R1 = (CH2)2O(CH2)2OH].

IT 111974-69-7P 329216-67-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of quetiapine, a dopamine antagonist)

RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (CA INDEX NAME)



RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)

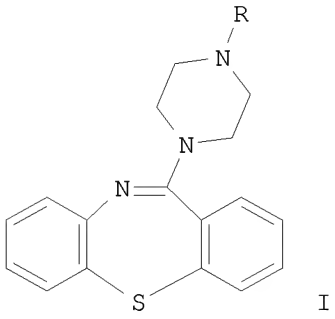


L13 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1114869 CAPLUS
DOCUMENT NUMBER: 145:397560
TITLE: Condensation process for the preparation of 11-[4-(substituted)-1-piperazinyl]dibenzo[b,f]-1,4-thiazepines from piperazines and 10H-dibenzo[b,f][1,4]thiazepin-11-one in the presence of titanium tetraalkoxides
INVENTOR(S): Comelv, Alexander Chris; Verdaguer Espaulella, Francesc Xavier; Rafecas, Jane Llorenc; Domingo Coto, Antonio
PATENT ASSIGNEE(S): Union Quimico-Farmaceutica S.A., Spain
SOURCE: Span., 16pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

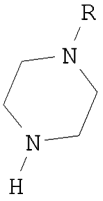
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2234447	A1	20050616	ES 2005-513	20050307
ES 2234447	B1	20060301		
WO 2006094549	A1	20060914	WO 2005-EP14055	20051221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1856073	A1	20071121	EP 2005-850361	20051221
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
US 20080171869	A1	20080717	US 2007-817884	20070906
NO 2007005071	A	20071128	NO 2007-5071	20071008

PRIORITY APPLN. INFO.:	ES 2005-513	A	20050307
	WO 2005-EP14055	W	20051221

OTHER SOURCE(S): CASREACT 145:397560; MARPAT 145:397560
GI



I



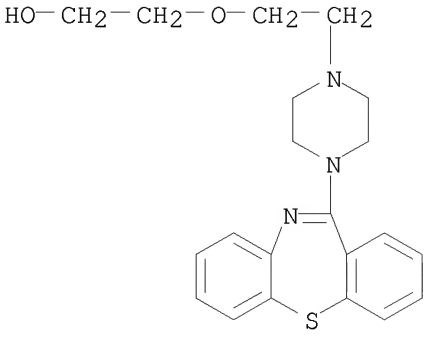
II

AB 11-[4-(Substituted)-1-piperazinyl]dibenzo[b,f][1,4]thiazepines [I; R = (CH2)2OH, (CH2)2O(CH2)2OH; e.g., quetiapine] are prepared by the condensation of piperazines [II; e.g., 1-(2-hydroxyethoxy)ethyl)piperazine] with 10H-dibenzo[b,f]-1,4-thiazepin-11-one in the presence of titanium tetraalkoxides Ti(OR1)4 [R1 = (un)branched C1-8 alkyl; e.g., titanium tetraisopropoxide] which may optionally be salified with acids.

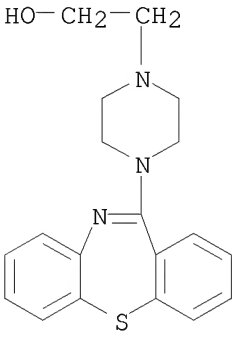
IT 111974-69-7P, Quetiapine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(condensation process for the preparation of 11-(4-substituted-1-piperazinyl)dibenzo[b,f]-1,4-thiazepines from piperazines and 10H-dibenzo[b,f][1,4]thiazepin-11-one in the presence of titanium tetraalkoxides)

RN 111974-69-7 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (CA INDEX NAME)



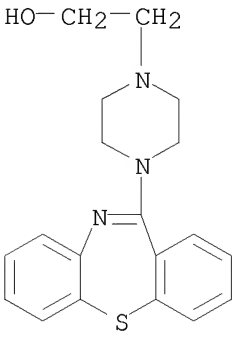
IT 329216-67-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(condensation process for the preparation of 11-(4-substituted-1-piperazinyl)dibenzo[b,f]-1,4-thiazepines from piperazines and 10H-dibenzo[b,f][1,4]thiazepin-11-one in the presence of titanium tetraalkoxides)
RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)



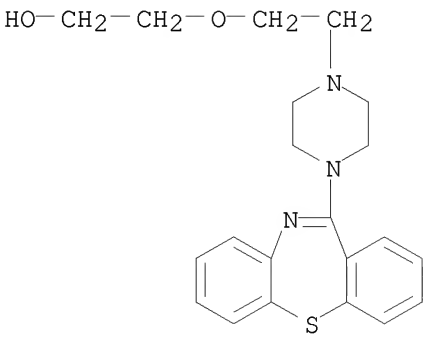
L13 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:684487 CAPLUS
DOCUMENT NUMBER: 145:327595
TITLE: In vitro studies on quetiapine metabolism using the substrate depletion approach with focus on drug-drug interactions
AUTHOR(S): Hasselstroem, Joergen; Linnet, Kristian
CORPORATE SOURCE: Centre for Basic Psychiatric Research, Aarhus University Hospital, Den.
SOURCE: Drug Metabolism and Drug Interactions (2006), Volume Date 2005, 21(3-4), 187-211
CODEN: DMDIEQ; ISSN: 0792-5077
PUBLISHER: Freund Publishing House Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The metabolism of the atypical antipsychotic quetiapine was investigated by in vitro methods. Pharmacokinetic parameters were determined in human liver microsomes and recombinant cytochrome P 450 measuring substrate depletion and product formation. The cytochrome P 450 isoenzymes CYP3A4 and CYP2D6 displayed activity towards quetiapine. The isoenzyme CYP2D6 played a minor role in the metabolism of quetiapine as CYP3A4 contributed 89% to the overall metabolism A Km value of 18 μM was determined by substrate depletion, suggesting linear kinetics under therapeutic conditions. Drugs known to inhibit CYP3A4, such as ketoconazole and nefazodone, displayed almost complete inhibition at low concns., whereas inhibitors of CYP2D6 do not seem to have a clin. relevant effect.

IT 329216-67-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(in vitro studies on quetiapine metabolism using the substrate depletion approach with focus on drug-drug interactions)
RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)



IT 111974-69-7, Quetiapine
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); BIOL (Biological study)
(in vitro studies on quetiapine metabolism using the substrate depletion approach with focus on drug-drug interactions)
RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (CA INDEX NAME)

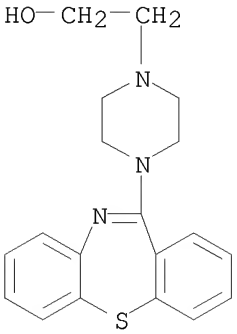


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

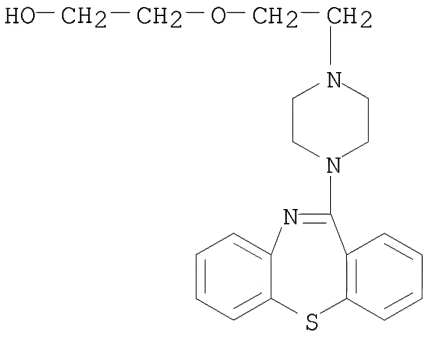
L13 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:238901 CAPLUS
DOCUMENT NUMBER: 144:292785
TITLE: Process for preparation of 11-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]dibenzo[b,f][1,4]thiazepine (Quetiapine) from 2-amino-2'-carboxydiphenyl sulfide and 1-hydroxyethoxyethylpiperazine.
INVENTOR(S): Pathak, Shailendra; Sharma, Jitendra; Kaushik, Geetesh; Thaper, Rajesh Kumar; Dubey, Sushil Kumar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006027789	A1	20060316	WO 2004-IN281	20040908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2006DN04348	A	20070713	IN 2006-DN4348	20060727
PRIORITY APPLN. INFO.:			WO 2004-IN281 W	20040908

OTHER SOURCE(S): CASREACT 144:292785
AB A process for preparation of Quetiapine comprises reaction of 2-amino-2'-carboxydiphenyl sulfide with a phosphorus halide or oxyhalide to give an iminohalide which is treated with 1-hydroxyethoxyethylpiperazine.
IT 329216-67-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Quetiapine from aminocarboxydiphenyl sulfide and 1-hydroxyethoxyethylpiperazine)
RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)

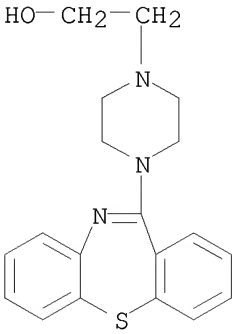


IT 111974-69-7P, Quetiapine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of Quetiapine from aminocarboxydiphenyl sulfide and 1-hydroxyethoxyethylpiperazine)
RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (CA INDEX NAME)

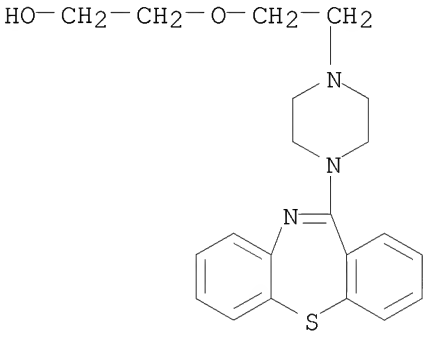


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:72863 CAPLUS
DOCUMENT NUMBER: 145:55319
TITLE: Effects of cytochrome P450 3A modulators ketoconazole and carbamazepine on quetiapine pharmacokinetics
AUTHOR(S): Grimm, Scott W.; Richtand, Neil M.; Winter, Helen R.; Stams, Karen R.; Reele, Stots B.
CORPORATE SOURCE: AstraZeneca Pharmaceuticals LP, Wilmington, DE, USA
SOURCE: British Journal of Clinical Pharmacology (2006), 61(1), 58-69
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aims To explore the potential for drug interactions on quetiapine pharmacokinetics using in vitro and in vivo assessments. Methods The CYP enzymes responsible for quetiapine metabolite formation were assessed using recombinant expressed CYPs and CYP-selective inhibitors. P-glycoprotein (Pgp) transport was tested in MDCK cells expressing the human MDR1 gene. The effects of CYP3A4 inhibition were evaluated clin. in 12 healthy volunteers that received 25 mg quetiapine before and after 4 days of treatment with ketoconazole 200 mg daily. To assess CYP3A4 induction in vivo, 18 patients with psychiatric disorders were titrated to steady-state quetiapine levels (300 mg twice daily), then titrated to 600 mg daily carbamazepine for 2 wk. Results CYP3A4 was found to be responsible for formation of quetiapine sulfoxide and N- and O-desalkylquetiapine and not a Pgp substrate. In the clin. studies, ketoconazole increased mean quetiapine plasma Cmax by 3.35-fold, from 45 to 150 ng ml-1 (mean Cmax ratio 90% CI 2.51, 4.47) and decreased its clearance (Cl/F) by 84%, from 138 to 22 l h-1 (mean ratio 90% CI 0.13, 0.20). Carbamazepine decreased quetiapine plasma Cmax by 80%, from 1042 to 205 ng ml-1 (mean Cmax ratio 90% CI 0.14, 0.28) and increased its clearance 7.5-fold, from 65 to 483 l h-1 (mean ratio 90% CI 6.04, 9.28). Conclusions Cytochrome P 450 3A4 is a primary enzyme responsible for the metabolic clearance of quetiapine. Quetiapine pharmacokinetics were affected by concomitant administration of ketoconazole and carbamazepine, and therefore other drugs and ingested natural products that strongly modulate the activity or expression of CYP3A4 would be predicted to change exposure to quetiapine.
IT 329216-67-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ketoconazole decreased formation of quetiapine metabolite O-desalkylquetiapine in healthy human)
RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)



IT 111974-69-7, Quetiapine
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(ketoconazole increased Cmax, AUC, t1/2, decreased CL/F of quetiapine in healthy human, carbamazepine decreased Cmax, AUC, tmax, increased CL/F of quetiapine in patient with psychiatric disorder)
RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-
(CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141066 CAPLUS
DOCUMENT NUMBER: 142:240472
TITLE: Procedure for preparing a pharmaceutically active compound
INVENTOR(S): Puig Torres, Salvador; Herbera Espinal, Reyes; Dalmases Barjoan, Pere
PATENT ASSIGNEE(S): Laboratorios Vita, S. A., Spain
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014590	A2	20050217	WO 2004-IB2527	20040727
WO 2005014590	A3	20050506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2223294	A1	20050216	ES 2003-1922	20030808
ES 2223294	B2	20051001		
EP 1660468	A2	20060531	EP 2004-744176	20040727
EP 1660468	B1	20070718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007501837	T	20070201	JP 2006-523068	20040727
AT 367383	T	20070815	AT 2004-744176	20040727
ES 2290734	T3	20080216	ES 2004-744176	20040727
US 20060189594	A1	20060824	US 2006-566413	20060130

PRIORITY APPLN. INFO.: ES 2003-1922 A 20030808
WO 2004-IB2527 W 20040727
OTHER SOURCE(S): CASREACT 142:240472; MARPAT 142:240472
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

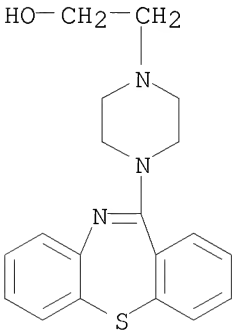
AB The invention relates to a procedure for preparing quetiapine (I) by reaction between dibenzothiazepine II and a compound P-OCH2CH2X [P = alc. protective group resistant to alkaline conditions; especially ethers, e.g., tetrahydropyranyl, CH2Ph, trityl; X = leaving group, e.g., halogen, mesylate, triflate, nonaflate, tresylate, tosylate, brosylate, nosylate], in the presence of a base, followed by a step of deprotection of ether III and, optionally,

obtaining a pharmaceutically acceptable salt thereof. Said procedure permits the obtaining of quetiapine with a high degree of purity under soft temperature conditions, with short reaction times and avoiding the use of toxic solvents.

IT 329216-67-3, 2-[4-(Dibenzo[b,f][1,4]thiazepin-11-yl)piperazin-1-yl]ethanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(etherification of, with (chloroethoxy)tetrahydropyran and analogs; procedure for preparing quetiapine from a dibenzothiazepine piperazinoethanol derivative)

RN 329216-67-3 CAPLUS

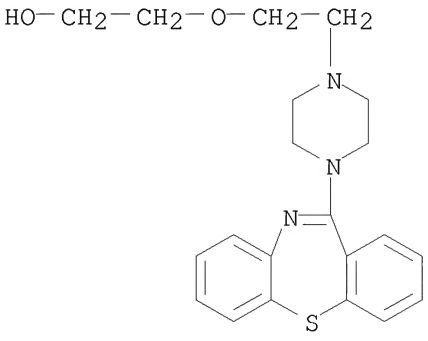
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)



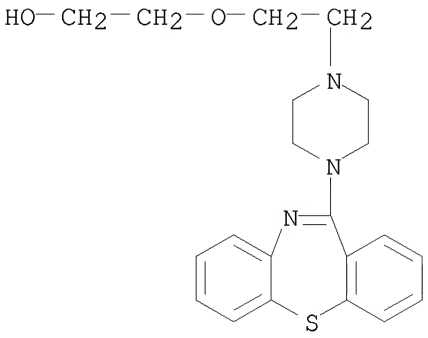
IT 111974-69-7P, Quetiapine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with fumaric acid; procedure for preparing quetiapine from a dibenzothiazepine piperazinoethanol derivative)

RN 111974-69-7 CAPLUS

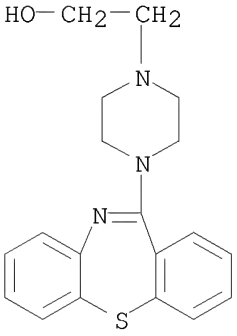
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (CA INDEX NAME)



L13 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:6274 CAPLUS
DOCUMENT NUMBER: 134:216805
TITLE: Behavioral Approach to Nondyskinetic Dopamine Antagonists: Identification of Seroquel
AUTHOR(S): Warawa, Edward J.; Migler, Bernard M.; Ohnmacht, Cyrus J.; Needles, Ann L.; Gatos, George C.; McLaren, Frances M.; Nelson, Cynthia L.; Kirkland, Karen M.
CORPORATE SOURCE: Departments of Medicinal Chemistry Pharmacology and Drug Disposition and Metabolism, AstraZeneca Pharmaceuticals LP, Wilmington, DE, 19850-5437, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(3), 372-389
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A great need exists for antipsychotic drugs which will not induce extrapyramidal symptoms (EPS) and tardive dyskinesias (TDs). These side effects are deemed to be a consequence of nonselective blockade of nigrostriatal and mesolimbic dopamine D2 receptors. Nondyskinetic clozapine (1) is a low-potency D2 dopamine receptor antagonist which appears to act selectively in the mesolimbic area. In this work dopamine antagonism was assessed in two mouse behavioral assays: antagonism of apomorphine-induced climbing and antagonism of apomorphine-induced disruption of swimming. The potential for the liability of dyskinesias was determined in haloperidol-sensitized Cebus monkeys. Initial examination of a few close congeners of 1 enhanced confidence in the Cebus model as a predictor of dyskinetic potential. Among dibenzodiazepines, 1 did not induce dyskinesias whereas its N-2-(2-hydroxyethoxy)ethyl analog was dyskinetic. The emergence of such distinctions presented an opportunity. Thus, aromatic and N-substituted analogs of 6-(piperazin-1-yl)-11H-dibenz[b,e]azepines and 11-(piperazin-1-yl)dibenzo[b,f][1,4]thiazepines and -oxazepines were prepared and evaluated. 11-(4-[2-(2-Hydroxyethoxy)ethyl]piperazin-1-yl)dibenzo[b,f][1,4]thiazepine was found to be an apomorphine antagonist comparable to clozapine. It was essentially nondyskinetic in the Cebus model. A number of N-substituted analogs were found to be good apomorphine antagonists but all were dyskinetic.
IT 111974-69-7P 329216-67-3P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinyl dibenzazepines as nondyskinetic dopamine antagonists)
RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (CA INDEX NAME)



RN 329216-67-3 CAPLUS
CN 1-Piperazineethanol, 4-dibenzo[b,f][1,4]thiazepin-11-yl- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT